AD_____
(Leave blank)

Award Number:
W81XWH-08-2-0038

TITLE:
The Effects of Explosive Blast as Compared to Post-Traumatic Stress Disorder on Brain Function and Structure

Principal Investigator: Scott Sponheim, Ph.D.

CONTRACTING ORGANIZATION:
Minnesota Veterans Research Institute
Minneapolis, MN 55417-2309

REPORT DATE:
April 2009

TYPE OF REPORT:
Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT:

X Approved for public release; distribution unlimited

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE *(DD-MM-YYYY)*	2. REPORT TYPE	3. DATES COVERED *(From - To)*
30-04-2009	Annual	1 Apr 2008-30 Mar 2009

4. TITLE AND SUBTITLE
The Effects of Explosive Blast as Compared to Post-Traumatic Stress Disorder on Brain Function and Structure

5a. CONTRACT NUMBER
W81XWH-08-2-0038

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Scott R. Sponheim

Email: scott.sponheim@va.gov

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Minnesota Veterans Research Institute

1 Veterans Drive

Minneapolis, MN 55417-2309

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research
and Material Command
Fort Detrick, Maryland
21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for public release; distribution unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT
The purpose of the present study is to better characterize and differentiate the effects of combat stress and explosive blast on the brain. To achieve this goal, we have been collecting extensive data on neural structure and functioning, including information on emotional health via clinical interviews and self-report measures, as well as information on brain structure and functioning via physiological measures and MRI data. Thus far, we have performed preliminary phone screens on several dozen individuals. We have consented and begun to study about half this number as participants. We have completed all study procedures with three participants. We have not yet analyzed our data because we are in the preliminary stages of data collection, but because the clinical presentations of individuals with psychological trauma symptoms (e.g., PTSD) and individuals with brain injuries are often very similar, the results of this study should add to clinicians' understanding of how to better diagnose and treat these different conditions.

15. SUBJECT TERMS
Blast, trauma, PTSD, brain, structure, function, Iraq

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
U	U	U	UU	13	19b. TELEPHONE NUMBER *(include area code)*

Table of Contents

Page

INTRODUCTION:

The clinical presentation of individuals with blast-related neural damage and post-traumatic psychopathology are markedly similar and thus a clear description of the direct consequences of explosive blast is complicated by the emotional and cognitive sequelae of psychological trauma. The inability to clearly demonstrate the basis of symptomatology has led to both confusion for the soldier and his or her loved ones, as well as difficulty prescribing effective treatments and developing interventions that return injured soldiers to adaptive functioning. In the current study, we will use sophisticated measures of neural function and structure to characterize brain injury from explosive blasts in a sample of Operation Iraqi Freedom (OIF) National Guard soldiers who returned from deployment in the fall of 2007. To fully characterize the effects of blast on the brain and differentiate them from post-traumatic stress disorder, we will contrast groups of soldiers exposed to blast with groups experiencing post-traumatic stress disorder. The study will provide a means for separating co-occurring conditions of brain injury due to explosive blast and post-traumatic psychopathology. Information that clarifies the basis of symptoms in blast-related brain injury and post-traumatic stress disorder will improve diagnostic separation of the two conditions. In summary, this investigation will improve the characterization of blast-related traumatic brain injury, describe the essential features of the condition in terms of neural function and structure to inform diagnosis, and characterize mechanisms of recovery after blast-related neural injury to allow the creation of interventions that return soldiers to maximum levels of functioning.

BODY:

Based on the statement of work please find below the milestones projected to occur within the first year and reports of progress with respect to each milestone.

1. Hire staff
    a. Our goal within the first year was to hire staff necessary for initiation and implementation of the study. We have hired a project coordinator and a research assistant to work exclusively on this study. These two individuals are responsible for recruitment and collection of clinical interview data of participants. In addition, we have hired individuals who are able to implement EEG and MRI tasks and begin processing of these data. This goal has been completed.

2. Obtain national and local regulatory approval
    a. A second goal within the first year was to obtain national and local regulatory approval. We have obtained final approval from the three committees relevant to implementation of our study (HRPO, the local Minneapolis VAMC IRB, and the University of Minnesota IRB). All three committees have approved all the procedures associated with our study.
    b. Although our project has received final approval from the HRPO, the VA IRB, and the University of Minnesota IRB, throughout the first year we have continued to make minor modifications to our protocol to streamline the process and ensure that we are collecting necessary data. These modifications, submitted to all three regulatory boards as amendments to the original protocols, have been submitted in order to streamline and improve our data collection process. Examples of amendments submitted to the three regulatory boards include:
        i. Addition of study personnel
        ii. Slight modifications to the EEG session
        iii. Accommodations for a sister study of neuropsychological function funded through a separate source and led by a different investigator.
        iv. Minor modifications to phone screen to determine subject eligibility for the study.
        v. Addition of necessary and brief data collection tools for the clinical characterization of subjects (e.g., self-report measures of alcohol use and social functioning)

3. Purchase supplies and equipment
    a. A third task of the first year of this study was to purchase necessary supplies and equipment for the study. This has included purchasing and setting up computers and phones to be used for the study, in addition to acquiring office space to perform clinical interviews and house our research personnel. We have purchased all the necessary equipment and

supplies to complete clinical interviews, self-report questionnaires, EEG tasks, and MRI. We have completed this task.

4. Augment EEG laboratory
    a. We have designed and implemented paradigms to use during our EEG procedures. We have also collaborated with a local expert on EEG paradigms and PTSD to determine a final task that would measures physiological response differences in individuals with and without PTSD. As part of this process, we have purchased necessary equipment to measure physiological response as participants complete this procedure within the EEG lab. Study personnel are being trained in the implementation of these paradigms.

5. Design and testing of MRI/DTI scanning protocols
    a. We have designed, tested, and implemented MRI scanning sequences for the acquisition of T1 and T2 structural scans and DTI scans. These data have been examined and determined to be of high quality.

6. Design and testing of EEG protocol
    a. We have also trained all study staff responsible for EEGs on the procedures to be used. For all EEG tasks, we have tested the study procedures. We have completed training and are now implementing the EEG tasks, which are running well.
    b. As mentioned above, we have collaborated with a local expert on EEG paradigms and physiological response to determine a final paradigm that would maximize differences in physiological response between individuals with and without PTSD. We have identified the paradigm and have ordered equipment needed to implement this task. We are in the process of training study staff to implement this task.

7. Clinical, MRI, and EEG staff trained
    a. During this year, all study staff have been trained in the necessary procedures. Our project coordinator and research assistant have been trained in administration of clinical interviews used in this study, such as the SCID-I and the CAPS interviews. These staff are also trained in procedures used to screen participants for inclusion in the study as well as how to schedule participants for lab visits.
    b. Other staff have been trained in administration of EEG tasks. We currently have three individuals on our staff who are able to administer the EEG tasks used in the study.
    c. We have also trained three individuals on administration of MRIs at the University of Minnesota. These individuals underwent CPR training and have learned how to screen individuals for metal in the body prior to undergoing the MRI. Three of our study staff have also been trained and are now implementing the MRI scanning procedures.

8. Data server purchased and operational
    a. Secure servers have been purchased, set-up, and tested in order to store study data and allow the analysis of clinical information as well as EEG and magnetic resonance imaging (MRI) variables. All study personnel have been trained on how to use these servers.
    b. Study personnel have also been trained in how to use and set up a relational database, which is a sophisticated means of linking different databases so that participant information remains accurate and current throughout the study. Our study personnel have created a relational database for use within this study. This database is now operational.

9. Telephone screen to obtain first 45 subjects
    a. Potential participants have been identified based on their responses to a mail survey in a related study. Data from this mail survey were used to identify a potential pool of participants. Participants who appear to meet study criteria, based on their responses to this mail survey, and who live within driving distance have been contacted via phone and invited to complete study a phone screen.
    b. Prior to implementation, the phone screen was piloted on other study personnel for length and appropriateness of questions. A detailed protocol to aid study personnel in screening and scheduling participants for this study has been created and implemented. As part of this protocol, we have determined appropriate inclusion and exclusion criteria for our study. During this year, we met regularly with experts in the field of traumatic brain injury in order to clarify the interpretation of inclusion and exclusion criteria so that we can maximize differences between participant groups (e.g., TBI versus no TBI) while still maintaining external validity of the study. Study personnel are now able to evaluate a potential participant's appropriateness for the study based on these criteria.
    c. During this year, we attempted to contact a total of 55 participants by phone to determine interest and eligibility for our study. We were unable to reach 7 participants due to lack of valid telephone numbers. 37 potential participants completed a phone screen with study personnel. Out of these, 11 were ineligible for our study, while 9 were not interested in participating. We continue to actively screen, recruit, and study subjects and anticipate meeting our total sample size goal.

10. Gather clinical, EEG, and MRI data on 1st cohort
    a. During this year, we have gathered clinical, EEG, and MRI data on participants based on responses during their phone screens. 16 participants have given informed consent for, are currently taking part in, and/or completed the study. Of these 16 participants, 11 are in the control group (no PTSD and no blast), while 2 individuals are in the blast only

group, 1 individual is in the PTSD only group, and 2 individuals are in the Blast + PTSD group.

b. In our Statement of Work, we had proposed to obtain data on a first cohort of 45 participants within the first year. Differences between what was originally proposed in the Statement of Work and the actual numbers of participants have been affected by:
    i. Recruitment of participants did not start until December 2008. At this rate, we have brought four participants into our lab per month, which is a rate that is consistent with what was proposed in our Statement of Work. The delay in initiation of study visits with participants was due to delays in receiving approval from the three regulatory boards. However, based on this rate, we plan to remain on task and complete our data collection in the allotted four years.
    ii. We were not able to start implementing the MRI portion of our study until March 2008, again due to the time needed to obtain approval from the regulatory boards in order to run the MRI scans. We do not anticipate that this will continue to be a problem, as we have now received approval to run these MRI scans.
c. In addition, the following numbers of participants have completed at least part of the study:
    i. 3 participants have completed all study procedures.
    ii. 16 Participants have been consented, provided a blood sample, and completed the clinical interview
    iii. 15 Participants have completed the self-report measures
    iv. 13 Participants have completed the EEG
    v. 3 Participant have completed the MRI

KEY RESEARCH ACCOMPLISHMENTS: Bulleted list of key research accomplishments emanating from this research.

- We expect that as a result of this research, both researchers and clinicians will be able to differentiate between clinical presentations of PTSD versus mild TBI. At this point, it is difficult to differentiate between the two disorders because their clinical presentations are similar. Additionally, the diagnosis of mTBI is not without controversy. We hope that our research will clarify differences between the two disorders, and thus lead to better treatment of the disorders.
- We have developed a consensus procedure for rating severity of brain injury due to blast and nonblast events based on the subjects self-report. The procedure yields quantitative indices reflecting the degree of cumulative insult to the brain due to events within and outside the military.
- EEG/physiological paradigms: We expect that as a result of this research, individual differences between participants with and without PTSD and participants with and without blast injury to their brain will emerge as a result of the paradigms that we have employed.

REPORTABLE OUTCOMES:

Dr. Scott Sponheim led a symposium at the EPIC XV congress on event-related potential research held in Bloomington, Indiana in mid April, 2009. The symposium presented a new measure of phase synchrony to an audience of researchers with expertise in the analysis of EEG data.

Dr. Scott Sponheim was invited to present at the International State-of-the-Science Meeting on Non-Impact, Blast-Induced Mild Traumatic Brain Injury (mTBI) on May 12-13, 2009. He will present on use of the phase synchrony measure with participants studied thus far.

Dr. Scott Sponheim has been invited to present at the Military Health Research Forum in September of 2009.

CONCLUSION:

The major accomplishments of the first year have been to set up the research lab, finalize protocols and procedures for data collection, receive final approval from the regulatory boards involved with the project, and to initiate data collection with our first cohort of participants. Currently, we have completed all tasks as planned, with the exception of collecting data on fewer participants than initially proposed in our Statement of Work. However, we have calculated the rates of data collection necessary to collect data on 180 participants within 30 months, which would give us a 6-month cushion at the end of the study. Given the remaining 30 months in which we would like to collect data, we have calculated that we will need approximately seven clinical visits per month, which will entail needing to perform phone screens on at least twice that many people per month. This data collection plan is well within our means, and we are confident that this plan will allow us to reach our goal of obtaining complete data within the allotted study period.

Because we are in the earlier stages of our data collection, we have yet analyzed data collected as part of this study. However, we expect that the data collected as part of this study will add to the literature by providing a better understanding of differences in memory and learning (e.g., differences in physiological measures, MRI data, EEG data, clinical measures, etc.) between individuals who have or have not been exposed to blast injury and those who do or do not have symptoms indicative of psychological trauma. In turn, we hope that these differences will help clinicians and researchers in the future be better able to differentially diagnose brain injuries versus psychological symptoms. The results of this study may also help military leadership and health care professionals be able to prescribe treatments, based on more accurate diagnosis of psychological versus organically based symptom presentations.

REFERENCES: List all references pertinent to the report using a standard journal format (i.e. format used in *Science, Military Medicine*, etc.).

None.

APPENDICES: Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.

None.